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3,5-DINITRO-1-(p-NITROPHENYL)-4-PYRIDONE AS A NOVEL PROTECTIVE GROUP OF PRIMARY AMINES

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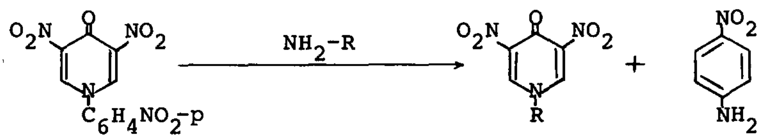
Summary: 3,5-Dinitro-1-(p-nitrophenyl)-4-pyridone is proposed as a novel protective group for primary amines, especially amino acids, based on the results of the transformation of 1-substituted 3,5-dinitro-4-pyridones with primary amines.

A novel ring transformation of 1-substituted 3,5-dinitro-4-pyridones with sodio β-keto esters has been reported.[1)] Now we wish to demonstrate the reactions of the 4-pyridones with various kinds of primary amines and their elegant utility for the amino protecting group.

Treatment of 3,5-dinitro-1-(p-nitrophenyl)-4-pyridone (DNPY-$C_6H_4NO_2$-p) with 1.1 equimolar amounts of isopropylamine in pyridine at room temperature gave 3,5-dinitro-1-isopropyl-4-pyridone [DNPY-$CH(CH_3)_2$] and p-nitroaniline, in good yield.

A variety of primary amines (NH_2-R) were easily modified by DNPY-$C_6H_4NO_2$-p to give 1-substituted 3,5-dinitro-4-pyridones (DNPY-R) quantitatively, liberating p-nitroaniline. The results are listed in Table 1.



(DNPY-$C_6H_4NO_2$-p) (DNPY-R)

Amino acids were also effective as the primary amine for this transformation, and gave corresponding DNPY-amino acids and p-nitroaniline.

Further, when the product, DNPY-Gly, was treated with aniline or propylamine in pyridine-water at room temperature, glycine was recovered in good yield together with either DNPY-C_6H_5 or DNPY-C_3H_7. Other amino acids could be recovered in theoretical yield from DNPY-amino acids under mild conditions as shown in Table 2. Racemization of the amino acids was not observed throughout the reactions.

$$\text{DNPY-amino Acid} \xrightarrow{NH_2\text{-R}} \text{Amino Acid} + \text{DNPY-R}$$

$$R = C_6H_5,\ CH_3,\ C_3H_7$$

Table 1 1-Substituted 3,5-Dinitro-4-pyridones (DNPY-R)[2)]

DNPY-R R	Molecular formula	Mp °C	Yield %	IR $\nu_{C=O}$ cm^{-1}	IR ν_{NO_2} cm^{-1}	NMR H_2 & H_6 ppm
$-CH_3$	$C_6H_5N_3O_5$	215-216	92.5	1680	1365, 1530	8.95
$-C_3H_7$	$C_8H_9N_3O_5$	235-236	81.5	1680	1350, 1540	9.12
$-CH(CH_3)_2$	$C_8H_9N_3O_5$	205-206	quant.	1685	1320, 1520	9.14
$-C(CH_3)_3$	$C_9H_{11}N_3O_5$	231-232	92.9	1700	1320, 1520	9.05
$-C_6H_{13}$	$C_{11}H_{15}N_3O_5$	122-123	81.4	1680	1335, 1525	9.13
$-(CH_2)_2OH$	$C_7H_7N_3O_6$	226-227	quant.	1680	1330, 1520	9.06
-cyclo-C_6H_{11}	$C_{11}H_{13}N_3O_5$	226-227	quant.	1685	1340, 1520	9.09
$-CH_2C_6H_5$	$C_{12}H_9N_3O_5$	192-193	89.4	1675	1330, 1540	9.22
$-C_6H_5$	$C_{11}H_7N_3O_5$	295-296	91.1	1675	1360, 1520	9.23
$-C_6H_4-CH_3$-p	$C_{12}H_9N_3O_5$	190-191	90.9	1680	1320, 1530	9.18
$-C_6H_4-CH_3$-o	$C_{12}H_9N_3O_5$	195-196	91.4	1690	1315, 1515	9.11
$-C_6H_4$-Cl-p	$C_{11}H_6N_3O_5Cl$	226-227	quant.	1690	1320, 1520	9.27
-2-pyridyl	$C_{10}H_6N_4O_5$	245-246	92.4	1675	1360, 1520	9.59
-3-pyridyl	$C_{10}H_6N_4O_5$	278-279	quant.	1685	1320, 1525	9.34
-2-pyrimidyl	$C_9H_5N_5O_5$	176-177	90.3	1680	1360, 1520	9.89
-Gly ($-CH_2COOH$)	$C_7H_5N_3O_7$	220 (dec.)	quant.	1690	1340, 1520	9.12
-L-Ala	$C_8H_7N_3O_7$	195 (dec.)	quant.	1690	1350, 1520	9.12
-L-Glu	$C_{10}H_9N_3O_9$	144 (dec.)	quant.	1675	1340, 1520	9.02
-L-Tyr	$C_{14}H_{11}N_3O_8$	195 (dec.)	quant.	1690	1350, 1520	9.03
-L-Ser	$C_8H_7N_5O_7$	196 (dec.)	quant.	1685	1340, 1535	9.12
-L-His	$C_{11}H_9N_5O_7$	255 (dec.)	quant.	1690	1340, 1525	9.04
$-L-AspNH_2$	$C_9H_8N_4O_8$	134 (dec.)	72.0	1690	1350, 1525	9.19

Table 2 Recovery of Amino Acids from DNPY-Amino Acids by Amines

DNPY-R	Amine	Amino Acid	Yield (%)	DNPY-R	Amine	Amino Acid	Yield (%)
DNPY-Gly	$PhNH_2$	Gly	70.0	DNPY-L-Leu	$MeNH_2$	L-Leu	quant.
DNPY-L-Ala	$MeNH_2$	L-Ala	quant.	DNPY-L-Glu	$PrNH_2$	L-Glu	quant.
DNPY-L-Ala	$PrNH_2$	L-Ala	quant.	DNPY-Gly-Gly	$PrNH_2$	Gly-Gly	80.0

The facts that the introduction and the removal of DNPY group were easily performed in mild conditions suggest 3,5-dinitro-1-(p-nitrophenyl)-4-pyridone to be useful for the protective group of the amino function of amino acid and others. These reactions also provide a convenient route for the preparation of 1-substituted 3,5-dinitro-4-pyridones. Further work is in progress.

References and Notes

1) E. Matsumura, M. Ariga, and Y. Tohda, Bull. Chem. Soc. Jpn., 53, 2891 (1980). cf. E. Matsumura, M. Ariga, and Y. Tohda, Tetrahedron Lett., 1979, 1393.

2) All compounds gave satisfactory analytical, IR, and NMR (in DMSO-d_6, TMS as the internal standard) data.

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